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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,645	12/04/2001	Satoh Yoshitaka	10624-050-999	6771

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EXAMINER	
KIM, JENNIFER M	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/004,645	YOSHITAKA ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 17, 27- 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 17, 27- 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/24/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The amendment filed on June 24, 2005 have been received and entered into the application.

Action Summary

The rejection of claims 1, 17 and 27 under 35 U.S.C. 112, first paragraph is maintained for the reasons stated in previous Office Action and modified herein to include claims 28-45.

Upon further consideration, additional rejection (Double Patenting rejection) has been made as follow:

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 17 and 27-45 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13, 14, 24-27, 38 and 39 of copending Application No. 10/004,642. Although the conflicting claims are not identical, they are not patentably distinct from each other because it encompasses same subject matter. The claims of instant Application differ from the co-pending Application regarding the treatment of various disorders by the inhibition of the JNK pathway. However, the mechanism of action of inhibition of JNK pathway by which the same active ingredient gives the same pharmacological effect does not alter the fact that the compound has been previously used to obtain the same pharmacological effects which would result from the claimed method. The patient, condition to be treated and the effect are the same. An explanation of why that effect occurs does not make novel or even unobvious the treatment of the conditions encompassed by the claims of copending Application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 17, 27-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "inhibition of the JNK pathway", does not reasonably provide enablement for the "treating" vast array of conditions including "atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method of treating a condition responsive to inhibition of the JNK pathway, comprising administering to a patient in need thereof an effective amount of a compound having the structure set forth in claims 1,17, 27-45 wherein the condition is atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial

infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure. The nature of the invention is extremely complex in that it encompasses the actual treatment of vast array of **unrelated conditions** such that the subject treated with above compounds does not contract all of the conditions set forth in claims 1, 17, 27-45 including atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass treatment of a complex unrelated conditions in humans which has potentially many different etiologies (i.e. many different mutations, combination of mutations, hereditary, drug-drug interaction, psychological etc.). Each of which may or may not be addressed by the administration of the claimed compounds and the mechanisms involving JNK pathway.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually treat any of the conditions set forth in claims 1, 17, 27-45 is minimal. All of the guidance provided by the specification is directed towards inhibition of JNK pathway rather than actual treatment of any of the unrelated disease conditions.

Working Examples: All of the working examples provided by the specification are directed toward the inhibition of JNK pathway rather than actual treatment of vast array of disease conditions set forth in claims 1, 17, 27-45.

State of the Art: While the state of the art is relatively high with regard to treatment of specific disorders (i.e. diabetes) with specific compound (anti-diabetic agent), the state of the art with regard to treatment of all of vast array of disease condition including atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure with a single moiety of compound is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to treat vast array of disease conditions including atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure. Further, To the extent that the application is directed to a method of treating atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease,

endotoxin shock, or multiple organ failure by inhibition of JNK pathway in vivo for the treatment of these vast array of conditions, which is highly speculative, a greater amount of evidence is required to show its operability in humans. It is to be noted that no data has been presented to establish that Applicants' compounds would act in the manner claimed as they relate to the treatment of vast array of compound in general by inhibition of JNK pathway in vivo. Moreover, a further study is needed to elucidate the role of JNK involvement in cardiac hypertrophy in vivo is evidenced by Yano et al. (abstract). Applicants' data has been reviewed but does not establish a correlation between the in-vitro tests performed and the use of the applicants active agents in-vivo for the treatment of vast array of conditions including atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual treatment of conditions including atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure in

a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of treating all of the conditions.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for treatment of atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard to treatment of atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given

the lack of significant guidance form the specification of prior art regarding actual treatment of atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy; Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to treat atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure in a subject by administration of one of the claimed compounds.

Therefore, a method of treating a condition responsive to inhibition of the JNK pathway, comprising administering an effective amount of a compound having the structure set forth in claims 1,17, 27-45 wherein the condition is atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure preventing in a subject is not considered to be enabled by the instant specification.

Response to Arguments

Applicants' arguments filed June 24, 2005 have been fully considered but they are not persuasive. Applicants argue that the JNK pathway is associated with numerous diseases, including cancer, inflammatory diseases and cardiovascular diseases and Applicants submit the additional peer-reviewed publications to demonstrate the correlation between particular claimed diseases and the JNK pathway. This is not persuasive because the diseases claimed have different known etiologies with different known treatments and the claimed compounds are variety of hereto substituted compounds and without showing viable data supporting the specific treatment employing the various active agents in an *in vivo* model, the correlation remains unclear. Without such data, the correlation is highly speculative. Therefore, the claimed subject matter remains non-enabled.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

Jmk
September 15, 2005